Brown[15] to yield crotyl alcohol, which was isolated by distillation (b.p. 118–119°, $n^{20}D$ 1.4263; lit.[15] b.p. 118°, $n^{20}D$ 1.4249). It formed a 3,5-dinitrobenzoate, m.p. 69.7–70°, lit.[14] m.p. 70°.

Free-Radical Reaction of Propylene Oxide.—One mole of propylene oxide (58.08 g.) and 0.01 mole of *t*-butyl peroxide (1.46 g.) were heated for 2 hr. as mentioned before. The unchanged propylene oxide was removed and allyl alcohol was identified in the remaining material by gas chromatography (2.0%; column A, 100°, 10 lb., 7.2 min.; and column C, 92°, 5 lb., 7.1 min.).

Free-Radical Reaction of Propylene Sulfide.—Propylene sulfide (0.50 mole, 37 g.) and 0.10 mole of *t*-butyl peroxide (14.6 g.) reacted for 2 hr. in a glass bomb as described previously. The black reaction mixture was distilled to remove the low-boiling material. Vacuum distillation (30–40° at 0.15 mm.) yielded 1.7 g. of higher boiling material and a large polymeric residue (approximately 20 g.). Product identifications were made as follows: thioacetone (0.15%; column D, 158°, 10 lb., 12 min.; and column E, 150°, 10 lb., 14.7 min.); allyl mercaptan (0.3%; column C, 87°, 8 lb., 6.5 min.; and column D, 74°, 6 lb., 3.3 min.); and allyl disulfide (0.84%; column D, 115°, 10 lb., 11.6 min.; and column E, 107°, 5 lb., 7 min.).

Preparation of Thioacetone.—Thioacetone was prepared by treating a solution of acetone and hydrochloric acid with hydrogen sulfide according to the method of Fromm and Baumann.[16] A yellow oil was obtained from steam distillation of the reaction mixture from which thioacetone trimer was obtained by distillation (b.p. 120–125 at 11 mm.; lit.[16] b.p. 130° at 13 mm.).

Preparation of Allyl Mercaptan.—Allyl mercaptan was prepared from an aqueous solution of allyl bromide and thiourea according to the method of Backer and Kramer.[17] It was purified by distillation (b.p. 66–68°, lit.[17] b.p. 67–69°).

Preparation of Allyl Disulfide.—Allyl chloride and sodium thiosulfate were caused to react to form the Bunte salt as repored by Westlake and Dougherty.[18] The Bunte salt was decomposed with hydrogen peroxide as described by Twiss.[19] Allyl disulfide was purified by distillation (b.p. 58–60° at 3.5 mm. lit.[20] b.p. 58–59° at 5 mm.).

Acknowledgment.—The authors wish to thank the National Institutes of Health, Public Health Service (CY-3691), and the Quartermaster Corps, U. S. Army (DA19-129-QM-1708), for their support of this work.

(15) S. W. Chaikin and W. G. Brown, *J. Am. Chem. Soc.*, **71**, 122 (1949).

(16) E. Fromm and E. Baumann, *Ber.*, **22**, 1035 (1889).

(17) H. J. Backer and J. Kramer, *Rec. trav. chim.*, **53**, 1102 (1934).

(18) H. E. Westlake, Jr., and G. Dougherty, *J. Am. Chem. Soc.*, **63**, 658 (1941).

(19) D. F. Twiss, *J. Chem. Soc.*, **105**, 36 (1914).

(20) L. D. Small, J. H. Bailey, and C. J. Cavallito, *J. Am. Chem. Soc.*, **69**, 1710 (1947).

The Syntheses of Tricyclic Systems with Nitrogen at a Bridgehead[1]

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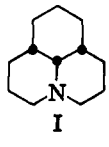
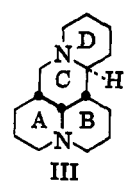
A facile synthesis of the all-*cis* isomer of hexahydrojulolidine is presented as well as its application to the preparation of other similar ring systems.

We have investigated the preparation of the all *cis* isomer of hexahydrojulolidine (I) as a model for the A, B, and C rings in the development of syntheses for matrine (II)[3] and matridine (III).[4]



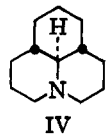
I

II

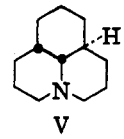


III

The three possible stereoisomers of hexahydrojulolidine, I, IV, and V, have been synthesized and characterized by Bohlmann[5] on the basis of their relative



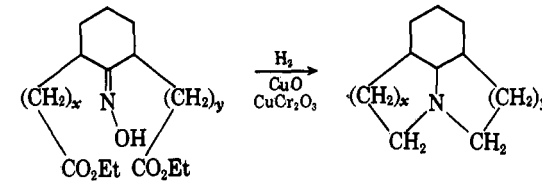
IV



V

rates of dehydrogenation as catalyzed by mercuric acetate, their very characteristic infrared spectral differences, and their behavior during chromatography.

We chose the work of Leonard and Middleton[6] as a pattern for the syntheses of these substances. Their approach involved the reductive cyclization of oximino diesters, as shown.



VI

Bohlmann demonstrated that in the case where $x = y = 2$ (hexahydrojulolidine) Leonard had incorrectly assigned the stereochemistry of his product as V and in fact the material prepared *via* this procedure was IV. Although this stereochemical consequence would appear to negate the application of Leonard's method of the synthesis of I, we felt that appropriate modification of the reduction conditions would allow formation of the all-*cis* product. An additional modification would be necessary for this approach to be applicable to a synthesis of matrine, II; namely, the reduction should not proceed *via* amide intermediates, as is probably the case in the reductive cyclization of oximino esters, for then the survival of the ring D lactam of matrine during reduction would be problematical.

Both of these requirements, milder reducing conditions and reduction intermediates not involving amides,

(1) First presented at the 138th National Meeting of the American Chemical Society, New York, N. Y., September, 1960. We wish to acknowledge the support of this research by the National Institutes of Health through Research Grant RG-7902.

(2) This work is taken in part from the Ph.D. dissertations of J. U. P. and K. P. S.

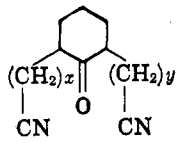
(3) L. Mandell, K. P. Singh, J. T. Gresham, and W. Freeman, *J. Am. Chem. Soc.*, **85**, 2682 (1963).

(4) L. Mandell, and K. P. Singh, *ibid.*, **83**, 1766 (1961).

(5) F. Bohlmann and C. Arndt, *Ber.*, **91**, 2167 (1958); F. Bohlmann, *ibid.*, **91**, 2157 (1958).

(6) N. J. Leonard and W. J. Middleton, *J. Am. Chem. Soc.*, **74**, 5114 (1958).

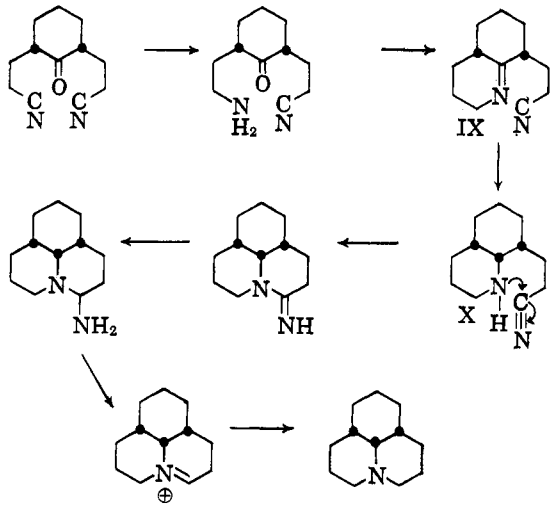
were met by using the keto dinitrile VII in place of the oximino diester in the reductive cyclization.[7]



VIIa, $x = y = 2$
b, $x = 1$; $y = 2$
c, $x = y = 1$

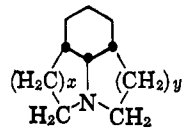
These substances were conveniently synthesized by utilizing Stork's enamine synthesis.[8] Thus the pyrrolidine enamine of cyclohexanone on treatment with acrylonitrile in alcohol affords VIIa. Compound VIIb was prepared by the alkylation of the pyrrolidine enamine of 2-cyanomethylcyclohexanone (itself prepared by the alkylation of cyclohexanone with chloroacetonitrile *via* the Stork procedure) with acrylonitrile.[9] Finally, VIIc was made available by alkylation of 2-cyanomethylcyclohexanone with chloroacetonitrile *via* the enamine process. The structures of VIIb and VIIc were confirmed by hydrolyses to the corresponding known keto diacids. On the basis of the method of synthesis one may assign the *more stable*, *cis* configurations to these 2,6-disubstituted (and hence diequatorially substituted) cyclohexanones.

We had anticipated that the reductive cyclization of these substituted cyclohexanones would take the following course (illustrated with VIIa).



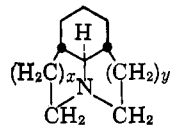
One would expect that, in the reduction of IX to X, hydrogen should add from the less hindered side of the molecule, which would be the side *trans* to the cyanoethyl grouping, to produce the all-*cis* isomer. In fact, this anticipation was realized. Reduction with Raney nickel in ethanol at 125° and 2300 p.s.i. gave a 68% yield of tertiary amine which was separated by chromatography into compounds I and IV in the ratio of 3:1, respectively. An improvement in the yield and stereospecificity was obtained by carrying out the reduction at room temperature in acetic acid solution at 60 p.s.i. with palladium catalysis. Under these conditions I was produced in 80% yield.

Reductive cyclizations of VIIb and VIIc were not so satisfactory as VIIa although little effort was expended in trying to develop the reaction. The low temperature and[4] pressure reaction was unsatisfactory; however, high temperature and pressure in the presence of Raney nickel gave XIb in 24% yield and XIc in 6% yield. These compounds were characterized as their

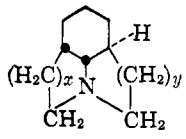


XIb, $x = 1$; $y = 2$
c, $x = y = 1$

picrates. Their infrared spectra exhibited prominent bands in the 3.55–3.70-μ region, attributed by Bohlmann to the presence of two hydrogens, on the carbon bearing the amine nitrogen, able to be transoid and coplanar to the "lone pair" nitrogen electrons. This would be possible in the structures XIb, XIc and structures XIIb, XIIc, but not structures XIIIb, XIIIc.



XIIb, $x = 1$; $y = 2$
c, $x = y = 1$



XIIIb, $x = 1$; $y = 2$
c, $x = y = 1$

Leonard[6] has synthesized a compound to which he has assigned structure XIIIb. Bohlmann's work[5] makes this structure unlikely and it would seem most probable that the hexahydrolilolidine synthesized by Leonard was XIIb. Our material was not identical with Leonard's isomer and on this basis we assign to it the structure XIb. This assignment is in accord with our synthesis of the all-*cis* hexahydrojulolidine (I) and the similarity in chromatographic behavior of XIb and I. Leonard's reduction of the appropriate oximino diester failed to yield any 1-azatricyclo[6.2.$10^{4,11}$]hendecane, (the 6,5,5 system) and hence our assignment of the all-*cis* configuration to XIc must be regarded as tentative.

Experimental[10]

Hexahydrojulolidine (I and IV).—A solution of 15 g. of cyclohexanone-2,6-dipropionitrile[8] in 100 ml. of absolute ethanol was hydrogenated in the presence of 5 g. of W-5 Raney nickel catalyst at 120–135° and an initial pressure of 1600 p.s.i. for 10 hr. The apparatus was allowed to cool overnight, the catalyst filtered off, and the ethanol removed *in vacuo*. The residue was fractionated to give a forerun below 100° which appeared to be a complex mixture of primary and secondary amines. The fraction boiling at 105–112° (3–4 mm.) was collected and weighed 9.0 g. (68%).

A solution of 9.0 g. of this crude product in 50 ml. of petroleum ether (b.p. 60–80°) was chromatographed on 250 g. of neutral alumina. The following fractions were collected: (A) ten 50-ml. portions of petroleum ether yielded 7.0 g. of I; (B) five 50-ml. portions of 50% petroleum ether–ether yielded 1.5 g. of IV

(7) Although reductive cyclization of keto nitriles to cyclic amines has been recorded, R. Longeray [A. Vigier, and J. Dreaux, *Compt. rend.*, **253**, 1810 (1960)], this work is the first instance of the reductive cyclization of a keto dinitrile to a bicyclic amine.

(8) G. Stork, A. Beizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(9) It is interesting that the reverse of this procedure, that is, introducing the three carbon chain first and then the two, failed, probably because of the lesser effectiveness of alkyl halides as alkylating agents as compared to electrophylic olefins.

(10) Melting points and boiling points are uncorrected. The infrared spectra were determined with a Perkin-Elmer Model 21 spectrophotometer fitted with a sodium chloride prism. The analyses are by Dr. G. Weiler and Dr. F. B. Strauss, Oxford, England.

and ten 100-ml. portions of ether yielded 0.5 g. of IV; and (C) five 10-ml. portions of 10% methanol–ether yielded no product.

The picrate of I melted at 218–220°, lit.[5] m.p. 225°. The picrate of IV melted at 188–189°, lit.[5] m.p. 186°.

Hexahydrojulolidine (I) from the Palladium Reduction.—A solution of 3.0 g. of cyclohexanone-2,6-dipropionitrile in 25 ml. of glacial acetic acid was hydrogenated in the presence of 1.0 g. of palladium on charcoal for 20 hr. at an initial pressure of 60 p.s.i. A drop in pressure equivalent to 0.069 mole (theoretical 0.074 mole) occurred. The catalyst was filtered off and the acetic acid removed *in vacuo*. The resulting material was diluted with 5 ml. of water and made basic to a pH of 12 with 15% sodium carbonate solution and concentrated sodium hydroxide solution. The basic solution was extracted with five 20-ml. portions of ether. The ether extracts were dried over magnesium sulfate and concentrated *in vacuo* giving 2.44 g. (93%) of material. Infrared analysis indicated that the product was approximately 90% *cis*-hexahydrojulolidine.

2-Oxocyclohexaneacetonitrile.—1-Pyrrolidinocyclohexene was prepared by refluxing 129 g. (1.32 moles) of cyclohexanone and 115 g. (1.6 moles) of pyrrolidine in 150 ml. of benzene under an azeotropic receiver for 8 hr. The benzene and excess pyrrolidine were removed by distillation, finally *in vacuo*, and the product used without further purification.

To this enamine in 100 ml. of acetonitrile was added over a period of 30 min. a solution of 100 g. (1.32 moles) of chloroacetonitrile in 100 ml. of acetonitrile. The resulting solution was stirred at room temperature overnight, refluxed for 1 hr., and concentrated *in vacuo*. After cooling, 150 ml. of 5% hydrochloric acid was added and the resulting mixture stirred at room temperature for 1 hr. The organic layer was separated and the aqueous layer extracted with three 75-ml. portions of ether. The combined organic layers were washed three times with 5% hydrochloric acid, twice with 5% sodium bicarbonate solution, and once with water. The ether solution was dried over magnesium sulfate and concentrated *in vacuo*. Distillation of the residue gave a forerun of starting materials and 64–80 g. (35–45%) of 2-oxocyclohexaneacetonitrile, b.p. 96–99° (1 mm.), lit.[11] b.p. 143–145° (12 mm.). The 2,4-dinitrophenylhydrazone derivative melted at 168–169°, lit.[11] m.p. 166.5–167°.

2-Cyanomethyl-6β-cyanoethylcyclohexanone (VIIb).—The pyrrolidine enamine of 2-oxocyclohexaneacetonitrile was prepared by refluxing 60.5 g. (0.44 mole) of the keto nitrile and 40 g. (0.56 mole) of pyrrolidine in 100 ml. of benzene under an azeotropic receiver for 12 hr. The benzene and excess pyrrolidine were removed by distillation, finally *in vacuo*, and the resulting product used without further purification.

A solution of this enamine in 100 ml. of absolute ethanol was cooled in an ice bath and a solution of 24 g. (0.45 mole) of acrylonitrile in 50 ml. of absolute ethanol was added. The ice bath was removed and the solution stirred at room temperature for 12 hr. The solution was then refluxed for 1 hr., cooled, 75 ml. of 5% hydrochloric acid added, and this mixture stirred for 1 hr. at room temperature. The product was isolated as for 2-oxocyclohexaneacetonitrile. Distillation gave 15.9 g. of the starting keto nitrile and 32.2 g. (38%) of the desired product as a light yellow oil, b.p. 174–176° (0.7 mm.).

Hydrolysis of a sample of the keto dinitrile with concentrated hydrochloric acid gave quantitatively the keto diacid, m.p. 166–168°, lit.[12] m.p. 167–168°.

2,6-Dicyanomethylcyclohexanone (VIIc).—A solution of 21.0 g. (0.28 mole) of chloroacetonitrile in 50 ml. of acetonitrile was added to a solution of the enamine of 2-oxocyclohexaneacetonitrile (from 41.6 g. of keto nitrile converted to enamine in the usual way) in 75 ml. of acetonitrile, and this was refluxed for 6 hr. After cooling, 100 ml. of 5% hydrochloric acid was added, and the mixture was stirred for 2 hr. The product was isolated as for 2-oxocyclohexaneacetonitrile. Distillation gave 26.0 g. of the starting keto nitrile and 5.0 g. (9.5%) of the desired product as a light yellow oil, b.p. 173–175° (1 mm.). The yellow liquid crystallized from ethanol to give a white solid, m.p. 66.0–66.5°.

Hydrolysis of a sample of the keto dinitrile with concentrated hydrochloric acid gave quantitatively the keto diacid, m.p. 186–187°, lit.[12] m.p. 188°.

Hexahydrolilolidine (XIb).—A solution of 10 g. of VIIb in 75 ml. of absolute ethanol was hydrogenated in the presence of 4 g. of W-7 Raney nickel catalyst at 145–155° and an initial pressure of 2300 p.s.i. for 10 hr. The apparatus was allowed to cool overnight, the catalyst filtered off, and the ethanol removed *in vacuo* leaving 8.5 g. of crude material. This was chromatographed on 60 g. of neutral alumina. Elution with 400 ml. of petroleum ether gave 5 g. of material, distillation of which gave two fractions boiling at 44–45° (0.2 mm.), 2.0 g., and 90–100° (0.2 mm.), 1.5 g.

The lower boiling fraction, contrary to the other, gave a crystalline picrate, m.p. 226–228° dec.

Anal. Calcd. for $C_{17}H_{23}N_4O_7$: C, 51.77; H, 5.62; N, 14.21. Found: C, 51.85; H, 5.94; N, 14.05.

1-Azatricyclo[6.2.1.0^{4,11}]hendecane (XIc).—A solution of 10 g. of VIIc was hydrogenated in the presence of Raney nickel as in the preparation of VI. Removal of the ethanol left 8.5 g. of crude product which was chromatographed on 60 g. of neutral alumina. Elution with 300 ml. of petroleum ether gave 4.8 g. of material which on distillation at 1 mm. gave three fractions: 0.5 g., b.p. 35°; 1.5 g., b.p. 76–77°; and 2 g., b.p. greater than 150°. The first fraction gave a crystalline picrate, m.p. 250–252° dec.

Anal. Calcd. for $C_{16}H_{21}N_4O_7$: C, 50.52; H, 5.30; N, 14.73. Found: C, 50.73; H, 5.41; N, 14.60.

(11) A. Dornow and E. Fleishmann, *Ber.*, **88**, 1340 (1955).

(12) G. Opitz, H. Mildenberger, and H. Suhr, *Ann.*, **649**, 47 (1961).

Free-Radical Additions to 2-Cyclopropylpropene[1]

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Received June 28, 1963

The peroxide- and light-induced additions of bromotrichloromethane and carbon tetrachloride to 2-cyclopropylpropene yield the 1,1,1-trichloro-3-methyl-6-halohex-3-enes as products. Addition of thiophenol to 2-cyclopropylpropene yields the unrearranged addition product, 1-thiophenoxy-2-cyclopropylpropane, whereas methyl mercaptan yields a mixture of the unrearranged and rearranged addition products, methyl 2-cyclopropylpropyl sulfide and methyl 2-methylpent-2-enyl sulfide, respectively. A mechanism is suggested to account for the products of these reactions. Competition reactions involving addition of thiyl radicals and trichloromethyl radicals to 2-cyclopropylpropene and 2,3-dimethyl-1-butene show that the cyclopropyl group enhances the reactivity of a double bond toward addition of these free radicals by a factor of about five.

The cyclopropylcarbinyl cation has received a considerable amount of attention from organic chemists because of its apparent ease of formation and its ability to undergo rearrangements.[3] The somewhat general parallel stabilities of carbonium ions and alkyl free radicals suggests that an unusual degree of stability might be found in the cyclopropylcarbinyl radical.

(1) This work was supported by Grant No. 512-A from the Petroleum Research Fund.

(2) Taken in part from the thesis submitted by J. D. T. in partial fulfillment of the requirements for the Ph.D. degree, University of Kansas.

(3) For a discussion of some of the chemistry concerning this system, see E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, pp. 588–590.